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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7 :
A61L 27/00, A61C 8/00, A61K 6/097

A1

(11) International Publication Number: **WO 00/04939**

(43) International Publication Date: 3 February 2000 (03.02.00)

(21) International Application Number: PCT/IE99/00074

(22) International Filing Date: 21 July 1999 (21.07.99)

(30) Priority Data:

S980594	21 July 1998 (21.07.98)	IE
S980595	21 July 1998 (21.07.98)	IE
S980596	21 July 1998 (21.07.98)	IE
S980597	21 July 1998 (21.07.98)	IE
S980598	21 July 1998 (21.07.98)	IE
S980599	21 July 1998 (21.07.98)	IE

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(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DE (Utility model), DK, DK (Utility model), EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published
With international search report.

(54) Title: DENTAL PIN

(57) Abstract

A dental pin for insertion into a cavity from which a tooth has been removed comprises a body to at least partially conform with the shape of the cavity after tooth extraction. The body is formed from a biocompatible haemostatic polysaccharide or a derivative thereof.

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DENTAL PIN

Introduction

The invention relates to a dental product.

The invention in particular involves the use of polyanhydroglucuronic acids and salts thereof. The term polyanhydroglucuronic acid and salts there of as used herein also includes copolymers thereof, especially with anhydroglucose. This is hereinafter referred to as PAGA.

Co-pending patent application PCT IE98/00004 describes particular polyanhydroglucuronic acids and salts thereof and a method of preparing such compounds. In particular therefore, the term polyanhydroglucuronic acids and salts thereof includes the acids and salts referred to in this co-pending application.

Statement of Invention

Various pressing moulds may be used to produce suitably shaped pins from polyanhydroglucuronic acids and salts thereof particularly as described in co-pending application PCT IE98/00004. Such pins may be used in stomatology as fillings of post-extractional tooth cavities to efficiently control excessive bleeding. A positive effect on the healing of such wounds also results. One advantage of pins prepared by this method is that the pressing method does not necessarily require use of adjuvants such as glycols, alcohols, or water, the presence of which may reduce the haemostatic activity.

The pins may with advantage include antibacterial components of the inorganic or organic cation type which may be bound to the COOH, OH, or both types of these groups present in the polymeric chain of polyanhydroglucuronic acids and

salts thereof to form salts or complex salts. Examples, of cations which may be used for this purpose are Zn^{2+}, Hg^{2+}, Ag^{+}, or Cu^{2+} ions, aminoglycosidic, aminoclitolic or chinolinic antibiotics, chlorohexidine or other amines having bactericidal or bacteriostatic effects. Alternatively, the pins may also include pharmacologically active substances not directly bound to the polymeric chain such as herb extracts, vitamins, or even substances listed physically admixed to the polyanhydroglucuronic acids and salts thereof.

The manufacture is simple and inexpensive since is involves one single production step; no contraction or cracking of pins manufactured by such a pressing process has been observed.

According to the invention there is provided a dental pin for insertion into a cavity from which a tooth has been extracted, the pin comprising a body to at least partially conform with the shape of the cavity after tooth extraction, the body being formed from a biocompatible haemostatic polysaccharide, or a derivative thereof.

Preferably the pin body has a tapered sidewall.

Ideally the pin body includes a substantially conical profile. Preferably the pin body is of generally frustro conical shape.

The pin body may have integral engaging means for engagement by a placement tool such as a tweezers. The engagement means may comprise a formation in or on the shaped body.

In one embodiment of the invention the formation comprises recess means in the pin body. The recess means preferably comprises a groove in the pin body.

The polysaccharide preferably contains glucuronic acid and is derived from starches, cellulose and gums, or is of microbial origin.

Most preferably the polysaccharide is a glucoronoglucane or an intermolecular complex thereof.

The body may include an adjuvant.

The adjuvant may be a bactericidal agent such as chlorohexidine or polyvinylpyrrolidone-iodine complex.

Alternatively or additionally the adjuvant is an antimicrobial agent, such as an antibiotic, for example of aminoglycosidic type such as gentamycin or amikacin.

Preferably the polysaccharide is derived from a starch, cellulose or gum, or is of microbial origin.

The polysaccharide material is polyanhydroglucuronic acid and/or biocompatible salts thereof, or copolymers thereof with a biocompatible intermolecular complex thereof.

Preferably the biocompatible intermolecular polymer complex is a complex of:

an anionic component comprising a linear or branched polysaccharide chain containing glucuronic acid; and

a non protein cationic component comprising a linear or branched natural, semi-synthetic or synthetic oligomer or polymer.

In this case preferably at least 5% of the basic structural units of the polysaccharide are glucuronic acid.

The cationic component contains nitrogen that either carries a positive charge or wherein the positive charge is induced by contact with the polysaccharidic anionic component. The cationic component in this case is selected from derivatives of acrylamide, methacrylamide and copolymers thereof. Preferably the cationic component is selected from polyacrylamide, copolymer of hydroxyethylmethacrylate and hydroxypropylmetacrylamide, copolymers of acrylamide, butylacrylate, maleinanhydride and/or methylmetacrylate.

The cationic component may be a cationised natural polysaccharide. Preferably the polysaccharide is a starch, cellulose or gum. The gum may be guargumhydroxypropyltriammonium chloride.

The cationic component may be a synthetic or semi-synthetic polyamino acid. In this case preferably the cationic component is polylysin, polyarginin, or α, β-poly-[N-(2-hydroxyethyl)-DL-aspartamide].

The cationic component may be a synthetic anti-fibrinolytic. The anti-fibrinolytic is preferably a hexadimethrindibromide (polybren).

Alternatively the cationic component is a natural or semi-synthetic peptide. The peptide may be a protamine, gelatine, fibrinopeptide, or derivatives thereof.

The cationic component may be an aminoglucane or derivatives thereof. Preferably the aminoglucane is fractionated chitin or its de-acetylated derivative chitosan. The aminoglucane may be of microbial origin or is isolated from the shells of arthropods such as crabs.

In a preferred embodiment the anionic component is polyanhydroglucuronic acid and/or bicompatible salts and/or copolymers thereof.

The polyanhydroglucuronic acid and salts thereof preferably contain in their polymeric chain from 8 to 30 per cent by weight of carboxyl groups, at least 80 per cent by weight of these groups being of the uronic type, at most 5 per cent by weight of carbonyl groups, and at most 0.5 per cent by weight of bound nitrogen. Preferably the polyanhydroglucuronic acid and salts thereof contain in their polymeric chain at most 0.2 per cent by weight of bound nitrogen.

Most preferably the molecular mass of the polymeric chain of the anionic component is from $1x10^3$ to $3x10^5$ Daltons, ideally the molecular mass of the polymeric chain of the anionic component ranges from $5x10^3$ to 1.5×10^5 Daltons.

In a preferred embodiment the content of carboxyl groups is in the range of from 12 to 26 per cent by weight, at least 95 per cent of these groups being of the uronic type.

The anionic component preferably contains at most 1 per cent by weight of carbonyl groups.

In one embodiment the carbonyl groups are intra- and intermolecular 2,6 and 3,6 hemiacetals, 2,4- hemialdals and C2-C3 aldehydes.

In one preferred embodiment the cationic component is gelatine.

In another preferred embodiment the cationic component is chitosan.

The dental pin may include at least one biocompatible biologically active substance.

The dental pin as claimed may alternatively or additionally include at least one biologically acceptable adjuvant.

We have now found that by preparing polymeric intermolecular complexes (IMC) of glucuronoglucanes, notably microdispersed PAGA, prepared especially. according to PCT IE 98/00004 it is possible to enhance the haemostatic effect of the final products on this basis and the properties of the temporary wound cover formed after the haemostasis is achieved such as its flexibility and resistance to cracking on movable parts of the body.

It is also possible to upgrade physicomechanical properties of the final products on this basis. Such IMCs make it possible to prepare application forms whose manufacture from a pure PAGA or their simple salts is extremely difficult. Such application forms includes non-woven textile-like structures or polymeric films. To modify or upgrade the physical mechanical properties it is sufficient to use even a relatively small amount of polymeric counterion while it is possible to obtain suitable application properties within a broad concentration range of the components. The ratio of the glucuronoglucane to polymeric counterion can be 0.99:0.01 to 0.01:0.99.

Another advantage of glucuronoglucane based IMCs is the possibility to control their biological properties such as varying the degree of haemostatis, resorption time, or immunomodulative properties, and the like.

Polymeric cations suitable to form IMCs with glucuronoglucanes prepared for example according to PCT IE 98/00004 may roughly be subdivided to the following groups:

1. Synthetic biocompatible nitrogen-containing oligomers and polymers.

a) Derivatives of acrylamide and methacrylamide and their copolymers [such as polyacrylamide, copolymer of hydroxyethylmetacrylate and hydroxypropylmetacrylamide, copolymer of acrylamide, butylacrylate, maleinanhydride, and methylmetacrylate, and the like], or else cationised natural polysaccharides such as starches, celluloses, or gums such as guargumhydroxypropyltriammonium chloride.

b) Synthetic or semi-synthetic polyaminoacids such as polylysin, polyarginin, α,β-poly-[N-(2-hydroxyethyl)-DL-asparamide. Synthetic antifibrinolytics hexadimethrindibromide (polybren) can also be included in this group.

2. Natural or semi-synthetic peptides such as gelatine, protamines, or fibrinopeptides, and their derivatives.

3. Natural aminoglucanes such as fractionated chitin and its de-acetylated derivative chitosan, of microbial origin or isolated from the shells of arthropods such as crabs.

In preparing IMCs on the basis of PAGA according to the invention these three groups of substances can be combined to obtain required properties of the final product.

In general it can be said that IMCs using substances from 1a and 1b would preferably be used to prepare various types of highly absorbant biocompatible dressing materials in the form of nonwovens, films, plasters, and pads.

IMCs using the substances from 2 and 3 may serve as efficient haemostatic agents for internal applications in the microfibrillar form, in the microdispersed form as

dusting powders, in the form of films, granules, tablets or non-woven textile-like structures. Those preparations also display antiadhesive properties.

We have also found out that in the form of film-like cell culture matrices the latter IMCs incorporating PAGA and salts thereof as prepared according to PCT IE 98/00004 have a favourable effect on the growth of fibroblasts and keratinocytes.

While it is also possible to create IMCs using structural scleroproteins of the collagen type as disclosed in WO 9800180A, it is preferable to use the above mentioned groups of substances because of the possibility of contamination of the final product by telopeptides, viruses or pyrogens. Collagen can affect in an uncontrolled manner, the immune response of the organism because formation of antibodies can be provoked by any portion of the collagen structure even though the main determinants occur in the terminal regions of the collagen macromolecule. Removal of telopeptides only partially solves the antigenicity problem (Michaeli et al: Science, 1969, 166, 1522).

By preparing IMCs according to the invention it is possible to essentially enhance properties of the originally prepared glucoronoglucanes such as 1,4 β PAGA. For instance an intermolecular complex salt of PAGA and gelatine in one single production step can be used to prepare final products in the form of a non woven, film, microdispersed granules, or dispersions. In contrast to collagen, suitably hydrolysed gelatine is well tolerated, has no toxicity or side effects and it is a much less costly raw material. We have found out that this complex has very good haemostatic properties being about 40% higher than the original PAGA calcium sodium salt. This is despite the fact that the gelatine itself only displays a haemostatic effect after an addition of thrombin [Schwartz S.I. et al.: Principles of Surgery, St.Louis: McGraw Hill Co, 1979, p. 122-123]. In this case the absorption in the organism can be controlled by changing the composition of the complex within the range from tens of hours to several months. With an

advantage this complex with a higher haemostatic efficiency can be used as an embolisation or microembolisation product. It can also be used to prepare haemostatic layers of highly absorbent multi-layer dressings or resorbable plasters, though more costly polybren or protamines could also be applied.

An important advantage of these IMCs is the fact that the compounds can be prepared within a single manufacturing operation using the hydrolytic process described in PCT IE 98/00004 which makes these products cost effective.

These IMCs can further be modified by biologically active and/or biologically acceptable substances. Because the IMCs prepared by the present procedure are either of a microdispersed or microfibrillar nature, the active substances tend to be bound uniformly and also are uniformly released in the organism without the need for other adjuvants such as micrcrystalline waxes or stearates. However, the addition of such adjuvants is not excluded.

Biologically active substances which can be incorporated into the IMC may involve, for instance, antibiotics carrying at least a weak positive charge in the molecule such as cephalosporins (cephotaxin), aminoglycosides (neomycin, gentamycin, amikacin), penicillins (tikarcilin) or macrolides (erythromycin, clarithromycin) and the like.

In cases where the calcium/sodium salt of PAGA or its IMC complexes according to the invention are used as microembolisation or embolisation agents in regional chemotherapy of malign tumours, suitable types of cytostatics such as adriamycin or derivatives of 1,4-diaminoanthrachinone can be incorporated. It is also possible to use the IMCs as detaching ligands for platinum(II) based cytostatics.

Biologically acceptable substances used for modification of the IMCs include, for instance, glycerol and its polymers (polyglycerols); mono, di, and certain triglycerides; polyethyleneglycols; monopropyleneglycol; block copolymers of polyethyleneoxides and polypropyleneoxides (Pluronic); starches; cyclodextrines; polyvinylalcohols; cellulose and its derivatives; in general, substances that, in the concentrations used, are not irritating or toxic for the living organism while being capable of further optimising the physicomechanical properties of the final product based on the IMCs according to the invention.

Detailed Description

The invention will be more clearly understood from the following description thereof given by way of examples only.

Examples of Polymer Complexes of Glucuronoglucanes

Example 1:

Material: long-fibre cotton – medicinal cotton wool oxidised by N_xO_y (proprietary)

C_6OOH 18.8 % b/w

ash content < 0.1 % b/w

$\sum C=O$ 0.6 % b/w

20% solution Na_2CO_3 (Lachema, a.s. Neratovice)

$CaCl_2.6H_2O$ anal.grade (Lachema, a.s. Neratovice)

demineralised water 2μS

ethanol, synthetic rectified conc. 98% (Chemopetrol Litvínov, a.s.)

acid acetic anal.grade (Lachema, a.s. Neratovice)

H_2O_2 anal.grade 30% (Lachema, a.s. Neratovice)

N-HANCE 3000 guargumhydroxypropyltriammoniumchloride (Aqualon – Hercules)

Equipment: mixer: bottom stirring, 150 l (duplicator), stainless steel EXTRA S
vibrating screen: stainless steel, 150 mesh
rotary air pump: rotor diameter 150 mm
turbostirrer: ULTRA TURAX (Janke-Kunkel)
beaker: 5 l
pH meter PICCOLO
thermocouple thermometer

Procedure:

30g of N-HANCE 3000 were placed into and 5 l beaker and 3 l of demineralised water 2μS were added. Contents of the beaker were intensely stirred for 30 minutes. The pH value was adjusted to less than 4.5 by addition of an acetic acid solution leading to a viscosity rise.

60 l of demineralised water 2μS were introduced into a mixer. Then 3 kg of $CaCl_2.6H_2O$ anal.grade were added and the contents heated up to a temperature of 50°C under stirring. On dissolution of the calcium chloride the stirring was interrupted and 2.7 kg of the raw oxidised cotton wool were introduced. The mixer was closed and the contents were agitated for 120 seconds. Then the pH value of the contents was adjusted by addition of a 20% solution of Na_2CO_3 to 6 – 6.5 and 13 kg of H_2O_2 30% were introduced. The fibre suspension was slowly agitated for 10 minutes. Then the pH value was readjusted to 4.5 – 5.0 and the prepared viscous solution of N-HANCE 3000 was introduced. The contents of the mixer were stirred intensely for 30 seconds. Subsequently 60 l of synthetic rectified ethanol conc. 98% were introduced into the mixer. After another 15 seconds from adding the ethanol the contents of the mixer were transferred onto a vibrating screen, and the supernatant. Liquid was filtered off. The filtration cake was redispersed in the mixer in 60 l of a mixture of 18 l of synthetic rectified ethanol

conc. 98% and 42 l of demineralised water 2μS. The fibre suspension was filtered again on the vibrating screen.

The isolated material thus prepared may further serve to prepare final products of the nonwoven type via a wet or dry process.

Analysis:

Ca content	4.0 % b/w
Na content	1.8 % b/w
Σ C=O content	0.0 % b/w
COOH content	20.7 % b/w

Example 2:

Material: oxidised short-fibre cotton (Linters – Temming) (proprietary)

C_6OOH 16.8 % b/w

ash content < 0.15 % b/w

Σ C=O 2.6 % b/w

20% solution Na_2CO_3 (Lachema, a.s. Neratovice)

$CaCl_2.6H_2O$ anal.grade (Lachema, a.s. Neratovice)

redistilled water (PhBs 1997)

ethanol, synthetic rectified conc. 98% (Chemopetrol Litvínov, a.s.)

isopropanol 99.9% (Neuberg Bretang)

H_2O_2 anal.grade 30% (Lachema, a.s. Neratovice)

gelatine (PhBs 1997)

Equipment: turbostirrer: ULTRA TURAX (Janke-Kunkel)

sulphonation flask 1 l

heater 1.5 kW

laboratory centrifuge: 4000 rpm

thermostated water bath

pH meter PICCOLO
glass thermometer
rotary vacuum dryer or hot-air dryer

Procedure:

Into a 1 l sulphonation flask equipped with a turbostirrer and a heater, 400 ml of redistilled H_2O were placed, 15.73 g of $CaCl_2.6H_2O$ were added and on dissolution, 40.0 g of 20% Na_2CO_3 solution were introduced under stirring. Subsequently, 50 g of oxidised Linters were added to the white emulsion formed and the contents were heated up to 95°C and the stirring intensity set to a maximum. After 10 minutes, 30 g of 30% H_2O_2 were added into the flask and the hydrolysis continued for another 10 minutes. The contents were then cooled down to 60°C on a water bath and the pH of the system was adjusted to a value of 4.5 – 5.0 by addition of 20% solution of Na_2CO_3. Furthermore, gelatine solution (10 g of gelatine in 70 g of redistilled H_2O) warmed up to 50°C was added and let to react for another 20 minutes. The flask contents were then cooled down to 30°C in a water bath and 626 ml of synthetic rectified ethanol conc. 98% were added gradually under intense stirring. The suspension of IMC thus formed was isolated using a laboratory centrifuge. The supernatant liquid was filtered away and the cake was redispersed into 250 ml of 50% ethanol. The system was centrifuged again and after the separation of the supernatant liquid, the IMC was redispersed into 250 ml of synthetic rectified ethanol conc. 98% and let to stay for 4 hours. It was then centrifuged again, redispersed into 99.9 % isopropanol, and let to stay for a minimum of 10 hours at 20°C. The gel formed was centrifuged again and the product was dried in a rotary vacuum dryer or a hot-air dryer.

The product can be used, for instance, for microembolisation, for preparation of haemostatic dusting powders, for manufacture of polymer drugs, e.g. based on cytostatics, or for preparation of spheric particles for macroembolisation.

Analysis:

content Ca	4.4 % b/w
content Na	2.7 % b/w
content Σ C=O	0.0 % b/w
content COOH	20.5 % b/w
content N	1.8 % b/w

Example 3:

Material: oxidised short-fibre cotton (Linters – Temming) (proprietary)

C_6OOH 16.8 % b/w

ash content < 0.15 % b/w

Σ C=O 2.6 % b/w

NaOH anal.grade (Lachema, a.s. Neratovice)

redistilled water (PhBs 1997)

ethanol, synthetic rectified conc. 98% (Chemopetrol Litvínov, a.s.)

isopropanol 99.9% (Neuberg Bretang)

H_2O_2 anal.grade 30% (Lachema, a.s. Neratovice)

gelatine (PhBs 1997)

Equipment: turbostirrer: ULTRA TURAX (Janke-Kunkel)

sulphonation flask 1 l

heater 1.5 kW

laboratory centrifuge: 4000 rpm

thermostated water bath

pH meter PICCOLO

glass thermometer

rotary vacuum dryer or hot-air dryer

Procedure:

Into a 1 l sulphonation flask equipped with a turbostirrer and a heater, 400 ml of redistilled H_2O were placed, and 8 g of NaOH were added. On dissolution, 50 g of oxidised Linters were added, the contents were heated up to 70°C and the stirring intensity set to a maximum. After 20 minutes, 40 g of 30% H_2O_2 were added into the flask, temperature was increased to 85°C, and maintained for another 10 minutes. The contents were then cooled down to 50°C on a water bath and gelatine solution (10 g of gelatine in 70 g of redistilled H_2O) warmed up to 50°C was added to the hydrolysate. The temperature was decreased to 25 – 30°C and the pH of the system was checked and adjusted to a value of 6.0 – 6.5. Subsequently, 626 ml of synthetic rectified ethanol conc. 98% were added gradually under intense stirring. The suspension of IMC thus formed was isolated using a laboratory centrifuge. The supernatant liquid was filtered away and the cake was redispersed into 250 ml of 50% ethanol. The system was centrifuged again and after the separation of the supernatant liquid, the IMC was redispersed into 250 ml of synthetic rectified ethanol conc. 98% and let to stay for 4 hours. It was then centrifuged again, redispersed into 99.9 % isopropanol, and let to stay for a minimum of 10 hours at 20°C. The gel formed was centrifuged again and the product was dried in a rotary vacuum dryer or a hot-air dryer.

The product can be used, for instance, for microembolisation, for preparation of haemostatic dusting powders, for manufacture of polymer drugs, e.g. based on cytostatics, or for preparation of spheric particles for macroembolisation.

Analysis:

Na content	3.8 % b/w
Σ C=O content	0.0 % b/w
COOH content	21.5 % b/w
N content	2.7 % b/w

Example 4:

Material: oxidised short-fibre cotton (Linters – Temming) (proprietary)
C_6OOH 16.8 % b/w
ash content < 0.15 % b/w
$\Sigma C=O$ 2.6 % b/w
20% solution Na_2CO_3 (Lachema, a.s. Neratovice)
$CaCl_2.6H_2O$ anal.grade (Lachema, a.s. Neratovice)
redistilled water (PhBs 1997)
ethanol, synthetic rectified conc. 98% (Chemopetrol Litvínov, a.s.)
isopropanol 99.9% (Neuberg Bretang)
H_2O_2 anal.grade 30% (Lachema, a.s. Neratovice)
chitosan, degree of deacetylation 92% (Henkel)

Equipment: turbostirrer: ULTRA TURAX (Janke-Kunkel)
sulphonation flask 1 l
heater 1.5 kW
laboratory centrifuge: 4000 rpm
thermostated water bath
pH meter PICCOLO
glass thermometer
rotary vacuum dryer or hot-air dryer

Procedure:

Into a sulphonation flask, 250 ml redistilled H_2O were placed, and 5 g of NaOH were added. On dissolution, 25 g of oxidised Linters were introduced under stirring, the temperature increased to 50°C and the stirring intensity set to a maximum. After hydrolysing for 15 minutes, 35 g of 30% H_2O_2 were gradually

added to the system and the temperature was maintained at 50°C for another 20 minutes. The content were cooled down to 30°C and 400 g of highly viscous 5% solution of chitosan were added. The flask contents were then intensely stirred for another 10 minutes, and the pH of the system was adjusted, by addition of NaOH, to a value of 7.0. Subsequently 300 ml of synthetic rectified ethanol conc. 98% were added under stirring. The suspension of IMC thus formed was isolated using a laboratory centrifuge. The supernatant liquid was filtered away and the cake was redispersed into 250 ml of 50% ethanol. The system was centrifuged again and after the separation of the supernatant liquid, the IMC was redispersed into 250 ml of synthetic rectified ethanol conc. 98% and let to stay for 4 hours. It was then centrifuged again, redispersed into 99.9 % isopropanol, and let to stay for a minimum of 10 hours at 20°C. The gel formed was centrifuged again and the product was dried in a rotary vacuum dryer or a hot-air dryer.

The product can be used, for instance, for microembolisation, for preparation of haemostatic dusting powders, for manufacture of polymer drugs, e.g. based on cytostatics, or for preparation of spheric particles for macroembolisation.

Analysis:

Na content	1.8 % b/w
Σ C=O content	0.0 % b/w
COOH content	10.4 % b/w
N content	2.8 % b/w

Example 5:

Material: oxidised short-fibre cotton (Linters – Temming) (proprietary)

C_6OOH 16.8 % b/w

ash content < 0.15 % b/w

Σ C=O 2.6 % b/w

NaOH anal.grade (Lachema, a.s. Neratovice)
HCl 39% anal.grade (Lachema, a.s. Neratovice)
redistilled water (PhBs 1997)
ethanol, synthetic rectified conc. 98% (Chemopetrol Litvínov, a.s.)
isopropanol 99.9% (Neuberg Bretang)
H_2O_2 anal.grade 30% (Lachema, a.s. Neratovice)
gelatine (PhBs 1997)
Ambroxol (H. Mack, Germany)

Equipment: turbostirrer: ULTRA TURAX (Janke-Kunkel)
sulphonation flask 2 l
heater 1.5 kW
laboratory centrifuge: 4000 rpm
laboratory pin mill ALPINE (35 000 rpm)
thermostated water bath
pH meter PICCOLO
glass thermometer
rotary vacuum dryer or hot-air dryer

Procedure:

Into a sulphonation flask, 400 ml redistilled H_2O were placed, and 8 g of NaOH were added. On dissolution, 50 g of oxidised Linters were introduced under stirring, the temperature increased to 70°C and the stirring intensity was set to a maximum. After hydrolysing for 20 minutes, 40 g of 30% H_2O_2 were gradually added to the system and the temperature was increased to, and maintained at, 85°C for another 10 minutes. The content were cooled down to 50°C in a water bath, and gelatine solution (2 g of gelatine in 70 g of redistilled H_2O) warmed up to 50°C was added to the hydrolysate. The temperature was decreased to 25 – 30°C and the pH of the system was checked and adjusted to a value of 1.6 – 1.8

by addition of 39% HCl. Under intense stirring, a solution of Ambroxol (25g of ambroxolium hydrochloride in 500 ml of redistilled H_2O) was added gradually. After agitating for 5 minutes the pH value was adjusted to 4.3 –4.6 by adding 5% NaOH solution, and 626 ml of synthetic rectified ethanol conc. 98% were added under intense stirring. The suspension of Ambroxol containing IMC thus formed was isolated using a laboratory centrifuge. The supernatant liquid was filtered away and the cake was redispersed into, subsequently, 800 ml of 60% ethanol and 250 ml of 98% ethanol, wherein it was let to stay for a minimum of 10 hours. The system was centrifuged again and the product was dried at 40°C in a rotary vacuum dryer or a hot-air dryer. A white to slightly yellowish powder was obtained and further desagglomerated on an Alpine pin mill.

The product serves for the preparation of a mucoregulatory drug with a prolonged action.

Analysis:

Na content	4.6 % b/w
Σ C=O content	0.0 % b/w
COOH content	14.8 % b/w
N content	1.9 % b/w

Example 6:

Material: oxidised short-fibre cotton (Linters – Temming) (proprietary)

C_6OOH 16.8 % b/w

ash content < 0.15 % b/w

Σ C=O 2.6 % b/w

20% solution Na_2CO_3 (Lachema, a.s. Neratovice)

$CaCl_2.6H_2O$ anal.grade (Lachema, a.s. Neratovice)

redistilled water (PhBs 1997)

ethanol, synthetic rectified conc. 98% (Chemopetrol Litvínov, a.s.)

isopropanol 99.9% (Neuberg Bretang)
H_2O_2 anal.grade 30% (Lachema, a.s. Neratovice)
gelatine (PhBs 1997)
gentamycin sulphate (MERCK)

Equipment: turbostirrer: ULTRA TURAX (Janke-Kunkel)
sulphonation flask 2 l
heater 1.5 kW
laboratory centrifuge: 4000 rpm
laboratory pin mill ALPINE (35 000 rpm)
thermostated water bath
pH meter PICCOLO
glass thermometer
hot-air dryer
lyophiliser (Leibold Heraus, Germany)

Procedure:

Into a 2 l sulphonation flask equipped with a turbostirrer and a heater, 400 ml of redistilled H_2O were placed, 15.73 g of $CaCl_2.6H_2O$ were added and on dissolution, 40.0 g of 20% Na_2CO_3 solution were introduced under stirring. Subsequently, 50 g of oxidised Linters were added to the white emulsion formed and the contents were heated up to 95°C and the stirring intensity set to a maximum. After 10 minutes, 30 g of 30% H_2O_2 were added into the flask and the hydrolysis was continued for another 10 minutes. The contents were then cooled down to 60°C on a water bath and the pH of the system was adjusted to a value of 4.5 – 5.0 by addition of 20% solution of Na_2CO_3. Furthermore, gelatine solution (10 g of gelatine in 70 g of redistilled H_2O) warmed up to 50°C was added and let to react for another 20 minutes. The flask contents were then cooled down to 30°C in a water bath and 40 g of gentamycin sulphate in 600 ml of redistilled H_2O were added gradually within 10 minutes. 626 ml of synthetic

rectified ethanol conc. 98% were then added gradually under intense stirring to the antibiotic containing IMC suspension formed. The suspension of IMC thus formed was isolated using a laboratory centrifuge. The supernatant liquid was filtered away and the cake was redispersed into 250 ml of 50% ethanol. The system was centrifuged again and after the separation of the supernatant liquid, the IMC was redispersed into 250 ml of synthetic rectified ethanol conc. 98% and let to stay for 4 hours. It was then centrifuged again, redispersed into 99.9 % isopropanol, and let to stay for a minimum of 10 hours at 20°C. The gel formed was centrifuged again and the product was dried in a rotary vacuum dryer or a hot-air dryer.

The product can be used, for instance, for the manufacture of a dusting powder or a powder spray for the treatment of infected wounds.

Analysis:

Ca content	2.4 % b/w
Na content	1.6 % b/w
Σ C=O content	0.0 % b/w
COOH content	9.6 % b/w
N content	2.7 % b/w

Example 7:

Material: long-fibre cotton – medicinal cotton wool oxidised by N_xO_y (proprietary)

C_6OOH 18.8 % b/w

ash content < 0.1 % b/w

Σ C=O 0.6 % b/w

20% solution Na_2CO_3 (Lachema, a.s. Neratovice)

$CaCl_2.6H_2O$ anal.grade (Lachema, a.s. Neratovice)

demineralised water 2μS
ethanol, synthetic rectified conc. 98% (Chemopetrol Litvínov, a.s.)
isopropanol 99.9% (Neuberg Bretang)
acid acetic anal.grade (Lachema, a.s. Neratovice)
H_2O_2 anal.grade 30% (Lachema, a.s. Neratovice)
N-HANCE 3000 guargumhydroxypropyltriammoniumchloride (Aqualon – Hercules)
polybren (hexadimethrindibromide) (FLUKA)
chlorhexidindigluconate

Equipment: mixer: bottom stirring, 150 l (duplicator), stainless steel EXTRA S
vibrating screen: stainless steel, 150 mesh
rotary air pump: rotor diameter 150 mm
turbostirrer: ULTRA TURAX (Janke-Kunkel)
beaker: 5 l
pH meter PICCOLO
thermocouple thermometer

Procedure:

30g of N-HANCE 3000 were placed into and 5 l beaker and 3 l of demineralised water 2μS were added. Contents of the beaker were intensely stirred for 30 minutes. The pH value was adjusted to less than 4.5 by addition of an acetic acid solution leading to a viscosity rise.

60 l of demineralised water 2μS were introduced into a mixer. Then 3 kg of $CaCl_2.6H_2O$ anal.grade were added and the contents heated up to a temperature of 50°C under stirring. On dissolution of the calcium chloride the stirring was interrupted and 2.7 kg of the raw oxidised cotton wool were introduced. The mixer was closed and the contents were agitated for 120 seconds. Then the pH value of the contents was adjusted by addition of a 20% solution of Na_2CO_3 to 6 –

6.5 and 13 kg of H_2O_2 30% were introduced. The fibre suspension was slowly agitated for 10 minutes. Then the pH value was readjusted to 4.5 – 5.0 and the prepared viscous solution of N-HANCE 3000 was introduced. The contents of the mixer were stirred intensely for 30 seconds. A solution of 35 g of chlorhexidine digluconate in 350 ml of demineralised water 2μS was then introduced slowly within 10 minutes. Within another 10 minutes, a solution of polybren containing 120 g of polybrenu in 1000 ml of demineralised water 2μS was added. Subsequently 60 l of synthetic rectified ethanol conc. 98% were introduced into the mixer. After another 15 seconds from adding the ethanol, the contents of the mixer were transferred onto a vibrating screen, and the supernatant. Liquid was filtered off. The filtration cake was redispersed in the mixer in 60 l of a mixture of 18 l of synthetic rectified ethanol conc. 98% and 42 l of demineralised water 2μS. The fibre suspension was filtered again on the vibrating screen.

The isolated material thus prepared may further serve to prepare, via a wet or dry process, final products of the nonwoven type having an enhanced haemostatic activity and a bactericidal effect.

Analysis:

Ca content	3.6 % b/w
Na content	1.9 % b/w
Σ C=O content	0.0 % b/w
COOH content	18.1 % b/w
N content	0.35 % b/w

Example 8:

Material: oxidised short-fibre cotton (Linters – Temming) (proprietary)

C_6OOH 16.8 % b/w

ash content < 0.15 % b/w

Σ C=O 2.6 % b/w

20% solution Na_2CO_3 (Lachema, a.s. Neratovice)

$CaCl_2.6H_2O$ anal.grade (Lachema, a.s. Neratovice)

redistilled water (PhBs 1997)

ethanol, synthetic rectified conc. 98% (Chemopetrol Litvínov, a.s.)

isopropanol 99.9% (Neuberg Bretang)

H_2O_2 anal.grade 30% (Lachema, a.s. Neratovice)

Chitosan, degree of deacetylation 92% (Henkel)

Clarithromycin lactobionan (Abbott Laboratories, Italy)

Equipment: turbostirrer: ULTRA TURAX (Janke-Kunkel)

sulphonation flask 1 l

heater 1.5 kW

laboratory centrifuge: 4000 rpm

thermostated water bath

pH meter PICCOLO

glass thermometer

rotary vacuum dryer or hot-air dryer

dialysing bag (regenerated cellulose)

lyophiliser (Leybold Heraus, Germany)

laboratory pin mill ALPINE (35 000 rpm)

Procedure:

Into a sulphonation flask, 250 ml redistilled H_2O were placed, and 5 g of NaOH were added. On dissolution, 25 g of oxidised Linters were introduced under stirring, the temperature increased to 50°C and the stirring intensity set to a maximum. After hydrolysing for 15 minutes, 35 g of 30% H_2O_2 were gradually added to the system and the temperature was maintained at 50°C for another 20 minutes. The content were cooled down to 30°C and 400 g of highly viscous 2% solution of chitosan, having a pH value of 3.5, were added. The flask contents

were then intensely stirred for another 10 minutes, and the pH of the system was adjusted, by addition of NaOH, to a value of 7.0. During another 10 minutes, a solution of clarithromycin (44 g of clarithromycin in 456 ml of redistilled H_2O) was introduced and the pH of the system was adjusted to a value of 7.0-7.5. Stirring was interrupted, the flask contents were transferred into a dialysing bag and dialysed against water for 48 hours. Subsequently the product was isolated by centrifugation, lyophilised, and disintegrated on the laboratory pin mill ALPINE.

The product can be used, for instance, to prepare tablets or granules efficient against Helicobacter pylori occurring in the gastrointestinal tract.

Analysis:

Na content	4.8 % b/w
Σ C=O content	0.0 % b/w
COOH content	18.8 % b/w
N content	0.7 % b/w

Example 9:

Material: oxidised short-fibre cotton (Linters – Temming) (proprietary)

C_6OOH 16.8 % b/w

ash content < 0.15 % b/w

Σ C=O 2.6 % b/w

NaOH anal.grade (Lachema, a.s. Neratovice)

redistilled water (PhBs 1997)

ethanol, synthetic rectified conc. 98% (Chemopetrol Litvínov, a.s.)

isopropanol 99.9% (Neuberg Bretang)

H_2O_2 anal.grade 30% (Lachema, a.s. Neratovice)

gelatine (PhBs 1997)

$Bi(NO_3).5H_2O$ (MERCK)

Equipment: turbostirrer: ULTRA TURAX (Janke-Kunkel)
sulphonation flask 2 l
heater 1.5 kW
laboratory centrifuge: 4000 rpm
thermostated water bath
pH meter PICCOLO
glass thermometer
rotary vacuum dryer or hot-air dryer

Procedure:

Into a sulphonation flask, 400 ml redistilled H_2O were placed, and 8 g of NaOH were added. On dissolution, 50 g of oxidised Linters were introduced under stirring, the temperature increased to 70°C and the stirring intensity was set to a maximum. After hydrolysing for 20 minutes, 40 g of 30% H_2O_2 were gradually added to the system and the temperature was increased to, and maintained at, 85°C for another 10 minutes. The content were cooled down to 50°C in a water bath, and gelatine solution (0.5 g of gelatine in 50 ml of redistilled H_2O) warmed up to 50°C was added to the hydrolysate. The temperature was decreased to 25 – 30°C and the pH of the system was checked and adjusted to a value of 1.6 – 1.8 by addition of 39% HCl. A freshly prepared solution of $BiNO_3$ (54 g of $BiNO_3.5H_2O$ in 746 ml of H_2O) was introduced and the temperature maintained for another 15 minutes. Then the temperature was decreased to 25 – 30°C and the pH of the system was checked and readjusted to a value of 5.5 – 6.0. 626 ml of synthetic rectified ethanol conc. 98% were then added gradually under intense stirring. to the formed. The BiO^+ containing IMC suspension thus formed was isolated using a laboratory centrifuge. The supernatant liquid was filtered away and the cake was redispersed into 250 ml of 50% ethanol. The system was centrifuged again and after the separation of the supernatant liquid, the IMC was redispersed into 250 ml of synthetic rectified ethanol conc. 98% and let to stay for

a minimum of 4 hours. It was then centrifuged again, redispersed into 99.9 % isopropanol, and let to stay for a minimum of 10 hours at 20°C. The suspension formed was then centrifuged again and the product was dried in a rotary vacuum dryer or a hot-air dryer.

The product can be used, for instance, to prepare dusting powders for wound treatment or tablets for treatment of gastrointestinal tract malfunctions.

Analysis:

Na content	1.9 % b/w
Σ C=O content	0.0 % b/w
COOH content	20.0 % b/w
N content	< 0.3 % b/w
Bi content	4.7 % b/w

Example 10:

Material: oxidised short-fibre cotton (Linters – Temming) (proprietary)

C_6OOH 16.8 % b/w

ash content < 0.15 % b/w

Σ C=O 2.6 % b/w

20% solution Na_2CO_3 (Lachema, a.s. Neratovice)

$CaCl_2.6H_2O$ anal.grade (Lachema, a.s. Neratovice)

redistilled water (PhBs 1997)

ethanol, synthetic rectified conc. 98% (Chemopetrol Litvínov, a.s.)

isopropanol 99.9% (Neuberg Bretang)

H_2O_2 anal.grade 30% (Lachema, a.s. Neratovice)

gelatine (PhBs 1997)

cimetidine hydrochloride (SPOFA)

Equipment: turbostirrer: ULTRA TURAX (Janke-Kunkel)
sulphonation flask 2 l
heater 1.5 kW
laboratory centrifuge: 4000 rpm
thermostated water bath
pH meter PICCOLO
glass thermometer
rotary vacuum dryer or hot-air dryer

Procedure:

Into a 1 l sulphonation flask equipped with a turbostirrer and a heater, 400 ml of redistilled H_2O were placed, 15.73 g of $CaCl_2.6H_2O$ were added and on dissolution, 40.0 g of 20% Na_2CO_3 solution were introduced under stirring. Subsequently, 50 g of oxidised Linters were added to the white emulsion formed and the contents were heated up to 95°C and the stirring intensity set to a maximum. After 10 minutes, 30 g of 30% H_2O_2 were added into the flask and the hydrolysis was continued for another 10 minutes. The contents were then cooled down to 60°C on a water bath and the pH of the system was adjusted to a value of 4.5 – 5.0 by addition of 20% solution of Na_2CO_3. Furthermore, gelatine solution (10 g of gelatine in 70 g of redistilled H_2O) warmed up to 50°C was added and let to react for another 20 minutes. The flask contents were then cooled down to 30°C in a water bath and a solution of cimetidine (36 g of cimetidine hydrochloride in 400 ml of redistilled H_2O) were added under intens stirring. The contents were intensely agitated for 10 minutes and 800 ml of synthetic rectified ethanol conc. 98% were then added gradually. The suspension of IMC thus formed was isolated using a laboratory centrifuge. The supernatant liquid was filtered away and the cake was redispersed into 250 ml of 50% ethanol. The system was centrifuged again and after the separation of the supernatant liquid, the IMC was redispersed into 250 ml of synthetic rectified ethanol conc. 98% and let to stay for 4 hours. It was then centrifuged again, redispersed into 99.9 %

isopropanol, and let to stay for a minimum of 10 hours at 20°C. The gel formed was centrifuged again and the product was dried in a rotary vacuum dryer or a hot-air dryer.

The product can be used, for instance, to manufacture tablets or granulates for the treatment of the gastrointestinal tract or other non-malignant ulcerations.

Analysis:

Ca content	4.4 % b/w
Na content	2.7 % b/w
Σ C=O content	0.0 % b/w
COOH content	20.5 % b/w
N content	2.1 % b/w

Example 11:

Material: IMC-MDOC complex (as per above Example 2)
[(2S;2R)-3-amino-2-hydroxy-4-phenylbutenoyl]-L-leucin (Bestatin) (Boehringer Mannheim, Germany)
redistilled water (PhBs 1997)
methanol, conc. anal.grade (Chemopetrol Litvínov, a.s.)
diethylether (Lachema, a.s. Neratovice)

Equipment: turbostirrer: ULTRA TURAX (Janke-Kunkel)
sulphonation flask 2 l
laboratory centrifuge: 4000 rpm
hot-air dryer

Procedure:

The IMC-MDOC complex as prepared in Example 2 above was redispersed into redistilled water in a sulphonation flask using a turbostirrer. A solution of Bestatin

in methanol was then added to the flask in an amount sufficient to yield a 10% b/w concentration of Bestatin in the resulting Bestatin-gelatine-MDOC complex. After thorough homogenisation, the suspension formed was isolated by centrifugation. The supernatant liquid ws filtered away and the filtration cake was redispersed into concentrated methanol again, centrifuged, redispersed in diethylether, and after being allowed to stay for 1 hour, it was dried in a hot-air dryer.

The product, a microdispersed form of a Bestatin-gelatine-MDOC complex, can be used, for instance, to prepare microembolisation agents used in regional chemotherapy of malignant tumours or flat dressing structures for wound treatment.

Example A : ***Preparation of dental pins with MDOC***

MDOC = Microdispersed oxidised cellulose

Material: MDOC, particle size 0.1 - 2.0µm, specific surface area 86m^2/g, COOH group content 22.2% b/w, Ca content 4.2 % b/w, Na content 3.8 % b/w

Equipment: tabletting machine (KORSCH EK 0, Berlin)

Procedure:

100 g of MDOC powder were introduced into the tabletting machine equipped with a set of special shaped moulds. The tabletting force was set at a value of 5 kN.

Result:

Dental pins of a cone frustrum shape, 15 mm in height and 7 mm in base diameter,

with lateral grooves to facilitate grasping the pin with tweezers.

Indication:

Treatment of massive postextractional bleeding.

Example B : ***Preparation of dental pins from IMC-MDOC complex containing bactericidal agent***

Material: IMC-MDOC complex

chlorohexidine digluconate (FEROSAN)

ethanol synthetic rectified 98%

Equipment: laboratory mixer 4000 rpm

tabletting machine (KORSCH EK 0, Berlin)

Procedure:

100 g of IMC-MDOC complex prepared according to Example 2 were placed into the mixer and a solution of 1.6 g of chlorohexidine digluconate in 20 g of ethanol was added while stirring. The mixture was homogenised for 120 second, and introduced into the tabletting machine equipped with a set of special shaped moulds, and the tabletting force was set at a value of 5 kN.

Result:

Dental pins of a cone frustrum shape, 15 mm in height and 7 mm in base diameter, with lateral grooves to facilitate grasping the pin with tweezers.

Indication:

Treatment of massive postextractional bleeding with simultaneous administration of a

bactericidal agent.

Example C : *Preparation of dental pins from IMC-MDOC complex with antimicrobial agent*

Material: IMC-MDOC complex containing chitosan

MDOC, particle size 0.1 - 2.0 μm, specific surface area 86 m^2/g, COOH group content 22.2% b/w, Ca content 4.2 % b/w, Na content 3.8 % b/w

polyvinylpyrrolidone-iodine complex PVP-I micronised (ISP-USA)

Equipment: laboratory mixer 4000 rpm

tabletting machine (KORSCH EK 0, Berlin)

Procedure:

50 g of IMC-MDOC complex, 49 g of MDOC and 1 g of PVP-I complex were placed into the mixer. The mixture was homogenised for 120 second, and introduced into the tabletting machine equipped with a set of special shaped moulds. The tabletting force was set at a value of 5 kN.

Result:

Dental pins of a cone frustrum shape, 15 mm in height and 7 mm in base diameter, with lateral grooves to facilitate grasping the pin with tweezers.

Indication:

Treatment of massive postextractional bleeding with simultaneous administration of an antimicrobial agent.

The invention is not limited to the embodiments hereinbefore described which may be varied in detail.

CLAIMS

1. A dental pin for insertion into a cavity from which a tooth has been extracted, the pin comprising a body to at least partially conform with the shape of the cavity after tooth extraction, the body being formed from a biocompatible haemostatic polysaccharide, or a derivative thereof.

2. A dental pin as claimed in claim 1 wherein the pin body has a tapered sidewall.

3. A dental pin as claimed in claim 2 wherein the pin body includes a substantially conical profile.

4. A dental pin as claimed in any preceding claim wherein the pin body is of generally frustro conical shape.

5. A dental pin as claimed in any preceding claim wherein the pin body has integral engaging means for engagement by a placement tool such as a tweezers.

6. A dental pin as claimed in claim 5 wherein the engagement means comprises a formation in or on the shaped body.

7. A dental pin as claimed in claim 6 wherein the formation comprises recess means in the pin body.

8. A dental pin as claimed in claim 7 wherein the recess means comprises a groove in the pin body.

9. A dental pin as claimed in any preceding claim wherein the polysaccharide contains glucuronic acid and is derived from starches, cellulose and gums, or is of microbial origin.

10. A dental pin as claimed in any preceding claim wherein the polysaccharide is a glucoronoglucane or an intermolecular complex thereof.

11. A dental pin as claimed in any preceding claim wherein the body includes an adjuvant.

12. A dental pin as claimed in claim 11 wherein the adjuvant is a bactericidal agent.

13. A dental pin as claimed in claim 12 wherein the bactericidal agent is chlorohexidine or polyvinylpyrrolidone-iodine complex.

14. A dental pin as claimed in any of claims 11 to 13 wherein the adjuvant is an antimicrobial agent.

15. A dental pin as claimed in claim 14 wherein the antimicrobial agent is an antibiotic.

16. A dental pin as claimed in claim 15 wherein the antibiotic is of aminoglycosidic type such as gentamycin or amikacin.

17. A dental pin as claimed in any preceding claim wherein the polysaccharide is derived from a starch, cellulose or gum, or is of microbial origin.

18. A dental pin as claimed in claim any preceding claim wherein the polysaccharide material is polyanhydroglucuronic acid and/or biocompatible salts thereof, or copolymers thereof or a biocompatible intermolecular complex thereof.

19. A dental pin as claimed in claim 18 wherein the biocompatible intermolecular polymer complex is a complex of:

an anionic component comprising a linear or branched polysaccharide chain containing glucuronic acid; and

a non protein cationic component comprising a linear or branched natural, semi-synthetic or synthetic oligomer or polymer.

20. A dental pin as claimed in any of claims 17 to 20 wherein at least 5% of the basic structural units of the polysaccharide are glucuronic acid.

21. A dental pin as claimed in claims 19 or 20 wherein the cationic component contains nitrogen that either carries a positive charge or wherein the positive charge is induced by contact with the polysaccharidic anionic component.

22. A dental pin as claimed in claim 21 wherein the cationic component is selected from derivatives of acrylamide, methacrylamide and copolymers thereof.

23. A dental pin as claimed in claim 22 wherein the cationic component is selected from polyacrylamide, copolymer of hydroxyethylmethacrylate and hydroxypropylmetacrylamide, copolymers of acrylamide, butylacrylate, maleinanhydride and/or methylmetacrylate.

24. A dental pin as claimed in claim 19 wherein the cationic component is a cationised natural polysaccharide.

25. A dental pin as claimed in claim 24 wherein the polysaccharide is a starch, cellulose or gum.

26. A dental pin as claimed in claim 25 wherein the gum is guargumhydroxypropyltriammonium chloride.

27. A dental pin as claimed in claim 19 wherein the cationic component is a synthetic or semi-synthetic polyamino acid.

28. A dental pin as claimed in claim 27 wherein the cationic component is polylysin, polyarginin, or α, β-poly-[N-(2-hydroxyethyl)-DL-aspartamide].

29. A dental pin as claimed in claim 19 wherein the cationic component is a synthetic anti-fibrinolytic.

30. A dental pin as claimed in claim 29 wherein the anti-fibrinolytic is a hexadimethrindibromide (polybren).

31. A dental pin as claimed in claim 19 wherein the cationic component is a natural or semi-synthetic peptide.

32. A dental pin as claimed in claim 31 wherein the peptide is a protamine, gelatine, fibrinopeptide, or derivatives thereof.

33. A dental pin as claimed in claim 19 wherein the cationic component is an aminoglucane or derivatives thereof.

34. A dental pin as claimed in claim 33 wherein the aminoglucane is fractionated chitin or its de-acetylated derivative chitosan.

35. A dental pin as claimed in claim 33 or 34 wherein the aminoglucane is of microbial origin or is isolated from the shells of arthropods such as crabs.

36. A dental pin as claimed in any of claims 19 to 35 wherein the anionic component is polyanhydroglucuronic acid and/or bicompatible salts and/or copolymers thereof.

37. A dental pin as claimed in any of claims 18 to 36 wherein the polyanhydroglucuronic acid and salts thereof contain in their polymeric chain from 8 to 30 per cent by weight of carboxyl groups, at least 80 per cent by weight of these groups being of the uronic type, at most 5 per cent by weight of carbonyl groups, and at most 0.5 per cent by weight of bound nitrogen.

38. A dental pin as claimed in claim 37 wherein the polyanhydroglucuronic acid and salts thereof contain in their polymeric chain at most 0.2 per cent by weight of bound nitrogen.

39. A dental pin as claimed in claim 37 or 38 wherein the molecular mass of the polymeric chain of the anionic component is from $1x10^3$ to $3x10^5$ Daltons.

40. A dental pin as claimed in claim 39 wherein the molecular mass of the polymeric chain of the anionic component ranges from $5x10^3$ to 1.5×10^5 Daltons.

41. A dental pin as claimed in any of the claims 37 to 40 wherein the content of carboxyl groups is in the range of from 12 to 26 per cent by weight, at least 95 per cent of these groups being of the uronic type.

42. A dental pin as claimed in any of claims 37 to 41 wherein the anionic component contains at most 1 per cent by weight of carbonyl groups.

43. A dental pin as claimed in any of claims 37 to 42 wherein the carbonyl groups are intra- and intermolecular 2,6 and 3,6 hemiacetals, 2,4-hemialdals and C2-C3 aldehydes.

44. A dental pin as claimed in claim 19 wherein the cationic component is gelatine.

45. A dental pin as claimed in claim 19 wherein the cationic component is chitosan.

46. A dental pin as claimed in any preceding claim including at least one biocompatible biologically active substance.

47. A dental pin as claimed in any preceding claim including at least one biologically acceptable adjuvant.

48. A dental pin substantially as herein before described with reference to the examples.

INTERNATIONAL SEARCH REPORT

'rnational Application No
PCT/IE 99/00074

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61L27/00 A61C8/00 A61K6/097

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61C A61K A61L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CHEMICAL ABSTRACTS, vol. 106, no. 8, 23 February 1987 (1987-02-23) Columbus, Ohio, US; abstract no. 55869, BOGDALKOVA, D. ET AL: "Experimental implantation of Traumacel dental pins on the base of carboxycellulose into the corium" XP002121261 abstract & SCR. MED. FAC. MED. UNIV. BRUN. PURKYNIANAE (1986), 59(5), 293-7 , --- -/--	1

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

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Date of the actual completion of the international search	Date of mailing of the international search report
2 November 1999	16/11/1999

Name and mailing address of the ISA	Authorized officer
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International Application No
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